THE AUTONOMIC NERVOUS SYSTEM IN THE LIGHT OF RECENT RESEARCH

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If we look for a definition of the sympathetic system we find a description of nerves and ganglia corresponding very nearly to the structures described by the old anatomists as the greater nervus intercostalis or nervus trisplanchnicus.

In 1723, Winslow considered three sympathetic nerves; the greater sympathetic or intercostal nerve, the middle sympathetic or vagus nerve, and the lesser sympathetic or facial nerve. Those nerves were considered as conveying the nervous impulses representing the sympathetic functions which were the manifestation of the vegetative life as opposed to the animal life. X. Bichat in 1830 was the first to establish a clear distinction between the two aspects of life, and in translating his text we read: "The functions of an animal are of two main types. Some represent a series of assimilations and excretions; through them, the living organism transforms intaken molecules into its own substance and eliminates them as soon as they become heterogenous. Through these functions the organism lives in itself. Through the other type of functions it lives in the surrounding world, it sees what exists about itself, it moves according to its desires and its sensations, and it is able to express its desires, its fears, its pains, and its joys.

"I call organic life the total of the first group of functions, because all organized living beings possess it and because the organic substratum is the only necessary condition of its existence. The second group of functions represents the animal life, so called because it is characteristic of all animals." Further on in the text, we find: "There is no such thing as the greater sympathetic nerve, it is just a grouping of small ganglionic systems with anastomotic branches."

Bichat's conception of the sympathetic system, except for a few points, represents our actual theory concerning the rôle of this system. His idea of the dependence of the animal and the organic life is to be modified considerably and we must give to the animal system some control of the organic activities.

Claude Bernard demonstrated the rôle of the sympathetic system in the regulation of organic processes such as glandular secretion, vasomotor activity, regulation of body temperature, etc.

The English school of physiologists has specialized in the study of the sympathetic nervous system and the data offered by Gaskell, Langley and a few others are numberless. To Langley we are indebted for the name "autonomic nervous system", as well as for a considerable number of studies on the visceral functions. With him begins the period of physiological experimentation on the sympathetic nervous system and his name overshadows that of all the physiologists who have studied visceral innervation during the last twenty or thirty years. Langley's denomination "autonomic nervous system" seems to have won the approval of most investigators. Among the numerous synonymous terms we have: "involuntary nervous system", "vegetative nervous system", "organic nervous system", "Lebensnerven", and "système nerveux organovégétatif".

The autonomic nervous system is a system of nerves and ganglia, in which three parts may be considered: (1) the sympathetic nervous system (thoracolumbar or orthosympathetic), formed by the prevertebral ganglionated chains, the communicating rami and the branches coming from these ganglia; (2) the parasympathetic nervous system (craniosacral or bulbosacral), representing a part of a few cranial nerves and possessing a function similar to that of the sympathetic system; (3) the intravisceral nervous system (metasympathetic), composed of the nervous structures located in the organs.

The anatomy, physiology, and pathology of the different parts of this system are extensively described and discussed in many publications, among which the most outstanding are those by Langley, Langdon Brown, Guillaume, L. R. Muller and Kuntz. The embryological aspect of the question is generally very briefly summarized or completely overlooked. Yet it represents the most logical approach to a real knowledge of the sympathetic system; the study of the origin and the development of it enables us to understand its nature and the differences between its different parts. The literature concerning this point is very extensive; a general survey of it can be found in the Quarterly Review of Biology, vol. V, 1930.

As far as the primary origin of the sympathetic elements is concerned, the earliest theory stated that the spinal nerves gave rise to the sympathetic cells by means of a proliferative reaction. This point of view has been entirely discarded during the last twenty years and is now of historical interest only.

The theory of the mesenchymal origin of the sympathetic elements was inaugurated by Remak in 1847 and found only a very limited number of advocates. It has recently received real support in the publication of Tello, who attempted to show that an important part of the sympathetic system came from a local differentiation of mesodermal elements. Numerous observers consider the neural crest and the spinal ganglia as the exclusive source of sympathetic cells, while others give the main rôle to the neural tube by means of migration along the motor roots. Both theories are supported by experimental studies, the results of which are diametrically opposite; they agree, however, in denying the mesodermal origin.

It is actually impossible to disregard any one of the last three mentioned theories and further embryological investigation is needed to elucidate the primary origin of the sympathetic elements.

If we take into special consideration the development of the visceral innervation, we find also a great deal of confusion, especially concerning the nervous supply of the digestive tract. The mesodermal origin of the intravisceral ganglion cells, the primary sympathetic contribution, and the importance of the vagus nerve have been emphasized by noted investigators and the field is entirely open to new researches.

Descriptive embryology is by itself unable to solve these intricate problems. Experimentation is the only way of defining accurately the origin and the development of the different parts of the autonomic system. Among vertebrates, the amphibians represent the ideal material for embryological experimentation and although the peripheral sympathetic system is poorly developed, we selected this object for our first group of experiments. Two different operations were performed and the comparison of their results with the study of normal embryos should give us definite ideas about the embryological development of the autonomic nervous system in frogs.

1. *Extirpation of the dorsal half of the spinal cord.* With iridectomy scissors, one can easily remove the dorsal half of the entire length of the spinal cord. In doing so the neural crest is removed and the ventral half of the cord remains uninjured. Frog embryos have been kept alive as long as forty-five days after this

operation. The microscopic study shows very clearly that the sympathetic prevertebral chains are absent; the motor nerves are normally developed but they lack sheath cells; the digestive tract does not show any intravisceral ganglion cells; and the chromaffin part of the adrenals is lacking. These experimental results, though convincing enough, do not meet the objections made to entirely negative results and consequently an inverse type of operation was carried out.

2. *Removal of the hindbrain.* After removing the hindbrain, the vagal ganglion can be found but there are no connections with the brain stem. This vagal ganglion, however, is not normal; the intestinal branch is entirely lacking. In spite of the absence of this visceral branch, neuroblasts do exist in the walls of the digestive tract; the prevertebral sympathetic chains are present and normally developed; and the adrenals show their cortical and chromaffin parts. These results suggest strongly a placodic origin for this vagal ganglion.

These two sets of experiments corroborate each other very strikingly and there can be no doubt about their results. The sympathetic elements originate from the neural crest and not from the ventral half of the spinal cord. The intestinal ganglion cells arise from the thoracolumbar sympathetic and not from the vagus nerve. The only part of the vagus nerve which is derived from the medullary neural crest is the so-called intestinal branch.

We know from the study of normal embryos that the medullary neural crest is directly continuous with the neural crest of the first segments of the spinal cord. From a morphological point of view, the visceral part of the vagus should be considered as directly homologous to the thoracolumbar sympathetic. We know, furthermore, that the dorsal nucleus of the vagus nerve is homologous to the intermediary cell column (lateral horn) of the spinal cord. The visceral innervation is thus given by a nervous system derived from one continuous primordium, the neural crest, and there is no need of distinguishing a thoracolumbar sympathetic from a vagal parasympathetic.

By use of material resulting from physiological studies, the arguments in favor of a distinction between the orthosympathetic and the parasympathetic systems in amphibians are rather poor and contradictory. Goltz, in 1872, showed that the destruction of the brain and the upper part of the spinal cord provoked marked contractions of the stomach and of the esophagus. The same result was obtained after section of both vagi and it represented, evidently, an inhibitory effect of the vagal centers. Stimulation of the peripheral end of the cut nerves increased the strength of the contractions; apparently section or stimulation of the vagi produced the same results. After section of the vagi, stimulation of the hindbrain provoked strong contractions of the stomach. The author explained this fact by admitting the existence of connections between the vagus centers and the thoracolumbar sympathetic nerves.

Steinach and Wiener have made a systematic analysis of the visceral innervation of the frog. The stimulation of the dorsal spinal roots provoked contractions of the different levels of the digestive tract. The second spinal pair innervated the middle part of the esophagus, the third pair the lowest part of the esophagus, the fourth pair the stomach, the fifth and sixth pairs the small intestine, etc. The normal motility of the digestive tract was independent of the vagus centers; removal of the hindbrain gave rise to a few contractions of the stomach during a very short period of time.

Other authors described an inhibition of the stomach after stimulation of the vagi and an inhibition of the small intestine as a result of stimulation of the splanchnic nerves. Recent investigators have shown that stimulation of the same nerve may produce inverse effects depending on the actual state of tonus of the organ. A contracted stomach will be relaxed and a relaxed stomach will contract after stimulation of the vagus nerve.

The physiological antagonism between the vagus and the thoracolumbar system is very difficult to understand on such a basis. Much emphasis has been placed on the selective action of drugs on the different parts of the autonomic system. Selective drugs, in the strict meaning of the word, do not exist; all the drugs we know produce inverse effects according to the dosage. Small doses of the most studied neurotropic substances, such as atropin, adrenalin, and pilocarpin, produce entirely different effects than those obtained by larger doses. One is even allowed to doubt most pharmacological results when we actually know that nicotin, always considered as paralysing the synaptic connection, has a totally different effect when used in stronger doses.

If we summarize the evidence we have in favor of a distinction between the orthosympathetic and the parasympathetic systems, we do not find any serious argument. There is no more difference between the vagus nerve and the thoracolumbar sympathetic nerves than between two functions of the same nerve.

The vagus nerve and the thoracolumbar nerves are two parts of the same nervous system to which the name of "autonomic nervous system" may be given in order to avoid the confusion brought up by the use of the word sympathetic. Instead of trying to find differences between these two parts, the physiological experimentation should be so oriented as to demonstrate similarities and relationships between them.

The interrelationship of the different organs has been explained by attempts of the organism to maintain a normal balance between the orthosympathetic and the parasympathetic systems. All the neurotropic drugs provoke a hypertonus of one or of both systems and the hypertonus or the hypotonus of the system gives clinical symptoms considered as a typical syndrome characteristic of disturbances of the different parts of the autonomic system.

Disturbances of the vagosympathetic equilibrium are not exclusively nervous in origin; they ordinarily are neuro-endocrin disturbances. Hyperglycemia for example, may be the result of an hypersympatheticotonia corresponding to the hyperfunction of the sympatheticochromaffin system or it may be the result of a hypoparasympatheticotonia resulting from a decrease of the function of the endocrin islets of the pancreas. Hypertonia of one system or hypotonia of the other gives the same final results. There are numerous ways of exploring the autonomic equilibrium of an individual. The oculocardiac reflex, the influence of breathing on heartbeat, the tolerance to carbohydrates, and the injection of neurotropic drugs give a clear picture of this balance. Its clinical importance has sometimes been exaggerated. In spite of the contradictory results given by the clinicians interested in this aspect of disease, there seems to be a sound fundamental part which we can not discard.

Whether or not, from the point of view of pathology, a distinction between orthosympathetic and parasympathetic is necessary is not known. The actual tendency is to consider general disturbances of the autonomic system rather than any one part of it. The autonomic nervous system seems to be one system, without any essential difference between its constituent parts.